Introduction to the Meeting

Hans Troedsson
Jose Martines

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Each year, approximately 4 million infants die worldwide before completing the first 28 days of life. This translates into seven newborn lives lost every minute or 10,000 every day. Almost all (98%) of these deaths occur in developing countries and most are caused by infectious diseases, such as sepsis and pneumonia, and complications of prematurity, birth asphyxia, and injuries. Additionally, there are many indirect causes of neonatal deaths, the most important of which is low birth weight (LBW). Between 40% to 70% of all neonatal deaths occur among those weighing less than 2500 g at birth. Other indirect causes of perinatal and neonatal deaths include poor status of maternal health and nutrition, malaria, and untreated maternal infections (sexually transmitted diseases, urinary tract infections, and chorioamnionitis). Failure to provide tetanus immunization to pregnant women leads to almost 300,000 deaths due to tetanus neonatorum. Maternal and fetal malnutrition, and failure to exclusively breast-feed also contribute prominently to the risk of early death. Inability to recognize severe illness in a newborn, poor care-seeking behavior, and inadequate access to good-quality medical care also underscore many deaths. Further underlying these direct and indirect causes is widespread poverty, illiteracy, and gender discrimination faced by both mothers and female children in developing countries.

Although efforts over the past decades have greatly reduced worldwide child mortality, there remains an unfinished agenda in neonatal survival. In many developing countries, neonatal mortality now accounts for over 60% of all infant mortality and over 30% of under-five deaths. Most of these deaths are preventable and are due to the failure to implement simple, known interventions and the failure to identify and address socioeconomic and cultural barriers to seeking and receiving care. Strategies to reduce neonatal deaths must be delivered where births and deaths take place, not only in health facilities, but also in the community and in the home.

In May 1999, an international meeting was convened in Baltimore, Maryland to examine the magnitude and determinants of perinatal and neonatal mortality, and to scrutinize existing interventions to reduce these deaths.[1] Since that time, research and program priorities have been developed,[1–3] and many activities have been started by a variety of multilateral institutions, bilateral and national agencies and their contractors, and private organizations to speed the development and delivery of programs and interventions, and plan and initiate research.

In this context, the World Health Organization's (WHO) Department of Child and Adolescent Health and Development, Save the Children Federation's (SCF) Saving Newborn Lives (SNL) Initiative sponsored by the Bill and Melinda Gates Foundation, and the Child Health Research Project of the United States Agency for International Development (USAID) sponsored a meeting in Kathmandu, Nepal, from April 29 to May 3, 2001, to discuss and plan research needed to develop and implement neonatal survival interventions in the community to reduce perinatal and neonatal deaths. The primary objectives of the meeting were:

- to review the results of recent research on neonatal health; and
- to enhance the coordination of planned community-based research by sharing basic information on study design, evaluation instruments and implementation schemes.

CURRENT PROGRAM ISSUES

Gary L. Darmstadt

Pregnancy-related complications lead to a majority of perinatal and neonatal deaths, and contribute to the ill health of surviving infants born prematurely or with LBW. Additionally, they also are the source of half-a-million maternal deaths and suffering or disability in millions of women worldwide. Interventions that can be implemented before birth to improve pregnancy outcomes, and decrease perinatal and neonatal mortality include expanding maternal immunization with tetanus toxoid, improving maternal nutrition, smoking cessation, adequate rest, providing presumptive malaria prophylaxis in endemic areas, implementing syphilis screening and treatment measures, and improving the diagnosis and treatment of urinary and reproductive tract infections. Furthermore, health education that includes birth preparedness regarding place of delivery and identity of a skilled birth attendant, counseling on breast-feeding, information on the signs of serious illness, and that which encourages women to seek care for themselves and their infants will also decrease deaths.

A principal problem linked to poor perinatal–neonatal outcomes in developing countries is the lack of skilled health care during delivery. Most infants are born at home, often with only the aid of an untrained traditional birth attendant (TBA), relative, or neighbor — when available. Labor and delivery are risky processes for both the mother and the baby. A skilled health provider is needed to provide essential care to the mother and newborn during labor and immediately following birth as well as in the first few postpartum

days when the majority of neonatal deaths occurs. This attendant is needed to ensure a clean delivery, resuscitate neonates who do not breathe at birth, ensure thermal protection, encourage immediate and exclusive breast-feeding, and provide presumptive treatment of neonatal eye infections. The following programs are urgently needed to reduce mortality due to obstetric complications: regular training of health workers and birth attendants to provide for a clean delivery; improving the identification and management of malpresentation and prolonged labor; recognition and referral of complicated cases to health center or hospital; combating the barriers to referral compliance, including transportation of mothers, care of other children and funds; and institution of perinatal and neonatal audits to improve care at hospitals and health centers. Prevention of mother-to-child transmission (MTCT) of HIV-AIDS is also urgently needed in endemic areas.

Following delivery, postpartum care is seldom available in the community for mother or baby. The first days after birth are particularly important for the health of the newborn. During a home visit, birth attendants and health workers must educate families to provide essential care to the mother and child, including: hygienic care for the umbilical cord, guarding against cold stress and hypothermia, and promoting early and exclusive breast-feeding. Other measures necessary to prevent further neonatal deaths during this period consist of skin-to-skin Kangaroo Mother Care for preterm infants and proper management of neonatal sepsis and other infections. Special attention must also be provided to LBW infants who need more intensive support to ensure proper feeding, maintenance of body temperature, and hygiene for prevention of infections.

Importantly, interventions must be developed with the participation of all interested parties from planning through implementation, including researchers, program implementers, policymakers, and donors. This will increase the knowledge of the program and its sense of ownership from the community to the national levels. Feedback from community members is also required to refine interventions, and the development of process indicators is crucial to the objective evaluation of program success and the identification of necessary improvements. All of these factors will ultimately affect the sustainability of the intervention after the initial sponsors withdraw support.

CURRENT RESEARCH ISSUES

Gary L. Darmstadt

Although research priorities vary according to regional conditions and needs, a number of basic priorities have been identified that will greatly contribute to our knowledge of the causes of perinatal and neonatal mortality and contribute toward the development of improved, cost-effective strategies for combating these preventable deaths.[2,3]

Knowledge of infectious disease epidemiology and etiology in developing-country neonates has been based almost entirely on studies of hospitalized patients, or on retrospective, verbal autopsy-based surveys, neither of which accurately reflects the burden of disease in the community. In order for the most effective preventative and treatment strategies to be designed, we need population-based data, which precisely identifies the relative importance and the antimicrobial susceptibility patterns of the agents infecting neonates. We also need case–control studies in the community to identify the principal risk factors for morbidity and mortality from neonatal infections, including organism-specific risk factors. Research is also needed on how to best deliver available vaccines in a cost-effective and sustainable manner and to develop new vaccines and strategies for maternal immunization. Lastly, we need to evaluate current infection control and antibiotic use policies in health facilities and determine their effects on neonatal outcomes and antibiotic resistance rates.

Integrated Management of Childhood Illness (IMCI) is being adapted for inclusion of the management of sepsis in the early neonatal period, and is poised to make major contributions to reducing infectious morbidity and mortality. It has been predicted that implementation of IMCI protocols will reduce the total global disease burden by 14%.[4] Priority research in design of diagnosis and management strategies include: identification of historical information and clinical signs and symptoms that are most predictive of the presence of serious neonatal illness; development of guidelines for use in identifying seriously ill neonates; and training and testing the abilities of community health workers, mothers, and other care givers to use the algorithm to identify seriously ill neonates. Additionally, tools developed and validated in WHO's Making Pregnancy Safer (MPS) and Integrated Management of Pregnancy and Childbirth (IMPAC) initiatives will contribute to improved diagnosis and treatment of illnesses in this population. To further refine IMCI to address perinatal and neonatal illness, it is necessary to understand the impact of traditional care practices, the behavioral determinants of and logistical barriers to care seeking, and how to better deliver community health programs.

An estimated 63% of infants are born at home in developing countries. In Bangladesh, over 90% of births occur at home.[5] To

provide the needed antenatal, obstetric, and maternal and newborn care in the early weeks after delivery, we must first determine existing practices and the reasons for those practices, identify barriers to care-seeking for illness, and use this information to design and evaluate behavior change interventions. Skilled health care must be provided at delivery, and we must evaluate the role of traditional birth attendants and community health workers in the provision of essential newborn care, including postpartum visitation. Priority research for community care of the pregnant woman and neonate also includes: strategies to improve access to emergency obstetric care; methods to increase referral rates to health centers or hospitals for complicated pregnancies and newborn illness; and design of packages of simple practices for the routine postpartum care of neonates born in the community.

Prolonged labor often results in asphyxia during delivery, which kills over 1 million neonates annually and causes encephalopathy and other disabilities in at least that number of surviving children.[6] We need to better understand the risk factors for and burden of this morbidity and mortality in the community, and provide skilled health care at birth to recognize and manage prolonged labor and malpresentation, and refer complicated cases to a health facility. Birth attendants must be skilled at recognizing, resuscitating, and referring asphyxiated newborns. Appropriate resuscitation strategies at the community level must also be designed and tested. Specific interventions to evaluate also include fetal monitoring and the use of partographs and management protocols at referral centers.

In 1994, 45 million pregnant women were living in malaria-endemic areas, with over 23 million in sub-Saharan Africa alone.[7] In settings of moderate to high malaria transmission, malaria may cause up to 30% of preventable LBW in newborns, and account for 3% to 5% of neonatal mortality in highly endemic regions.[7,8] Although WHO recommends antimalarial drugs for prevention of malaria in pregnant women in endemic areas, many pregnant women at risk do not receive appropriate prevention or treatment as part of prenatal care. Research priorities for malaria prevention and treatment include: efficacy studies of presumptive, intermittent treatment to prevent malaria as part of routine antenatal care in areas of high malaria transmission; design of methods for treatment of malaria during pregnancy using safe, effective and simple regimens in areas of high, medium, and low malaria transmission; evaluation of the safety and efficacy of newly available antimalarial drugs (alone or in combinations) for malaria treatment and prevention in pregnancy; and reduction of malaria exposure during pregnancy using methods such as insecticide-impregnated bed nets.

Intrauterine growth retardation (IUGR) and preterm birth are two common forms of LBW in the world. Specific research activities to reduce LBW include: identification of simple methods for detection and treatment of bacterial vaginosis; development of strategies to improve knowledge and practice of methods to prevent sexually transmitted diseases; evaluation of the safety and efficacy of maternal caloric supplementation for reducing LBW; development of methods to reduce maternal anemia through the use of iron-folate supplements, antihelminthics and antimalarials; and evaluation of micronutrient supplementation (vitamin A, zinc, or combinations of micronutrients) for the reduction of LBW and/or neonatal morbidity and mortality.

Over 12 million women have been infected with HIV since the start of the epidemic and women now account for over 42% of the 30.6 million adults living with HIV-AIDS.[9] Maternal HIV-AIDS infection also increases the risk for stillbirth, spontaneous abortion, preterm birth, and LBW[1] (Table 1). Furthermore, an estimated 600,000 children are infected by their mothers in the perinatal and neonatal periods each year.[9] Without preventive treatment, up to 40% of children born to HIV-positive women will be infected.[10] Of those who are infected through MTCT, it is believed that about two-thirds are infected during pregnancy and around the time of delivery, and about one-third are infected through breast-feeding. To combat perinatal and neonatal transmission of HIV, we need to have better case definition and diagnostic signs; design optimal therapeutic drug regimens, such as single-dose nevirapine; further evaluate the role of chlorhexidine for the cleansing of the vagina and newborn skin; determine safe feeding practices for infants of women with known infections in high- and low-prevalence areas;[11–13] determine if micronutrient supplementation is helpful in averting infection in high-risk newborns; and develop strategies for prophylaxis of opportunistic and severe bacterial infections. Additionally, we need to

Table 1 Effects of Maternal HIV Infection

	Abortion	Stillbirth	Preterm births	Low birth weight	Small for gestational age	Neonatal mortality
Zambia	–	–	–	OR 3.8	NA	NA
Congo	NA	–	–	OR 7.9	NA	▲
Zaire	NA	▲	▲	▲	NA	OR 5.0
Kenya	NA	–	NA	OR 3.0	NA	NA
Malawi	–	–	–	–	–	NA
Kenya	OR 3	OR 2.1–2.9	OR 2.1	▲	OR 2.3	NA
Rwanda	NA	NA	–	▲	NA	–
Zimbabwe	NA	RR 1.6	NA	NA	NA	RR 2.7

Adapted from Nicoll A, et al. AIDS 1994; 8: 995–1005.

conduct more research on the immunological response to vaccines, and to evaluate whether certain vaccines, such as BCG should be postponed.

BURDEN AND DETERMINANTS OF PERINATAL AND NEONATAL MORTALITY

Jelka Zupan

The burden of disease from perinatal and neonatal mortality is high. It is partly hidden because of underreporting of fetal and early neonatal deaths. It is estimated that each year, nearly 4 million children die before or during birth and 4 million more die in the first month of life (neonatal period). Overall, the loss of healthy life from neonatal mortality represents an estimated 8.2% in sub-Saharan Africa and 13.6% in South Asia of the burden of disease.[14] Birth asphyxia and trauma, severe infections and complications of prematurity are the principal causes of neonatal deaths[15] (Figure 1). Stillbirths, however, are largely caused by complications in pregnancy and delivery including maternal infections, eclampsia, and complications during delivery.

In the past 20 years, postneonatal mortality rates in developing countries have decreased dramatically from 44/1000 live births to 24/1000 — largely due to the success of public health interventions, although improvement in general economic status has also made a major impact. During the same period neonatal mortality decreased little, from 44 to 39/1000 live births.

Underlying a substantial proportion of neonatal deaths is the problem of LBW. Important determinants of LBW are maternal poor health and undernutrition throughout her life, complications of pregnancy, and endemic diseases such as malaria and syphilis. Importantly, the problem of LBW is intergenerational: LBW infants remain poorly nourished during childhood and grow up to be stunted adults who in turn give birth to small infants. Thus, LBW must be combated at several points during the life cycle.

Regional and subregional estimates of LBW vary widely, but the largest burden of LBW lies in southern Asia with approximately 30% of babies born with LBW (Figure 2). The past two decades have seen little real improvement in LBW rates, around 1–2% per 10 years.

Another factor contributing to high rates of perinatal and neonatal mortality is inadequate care in the first days of life.

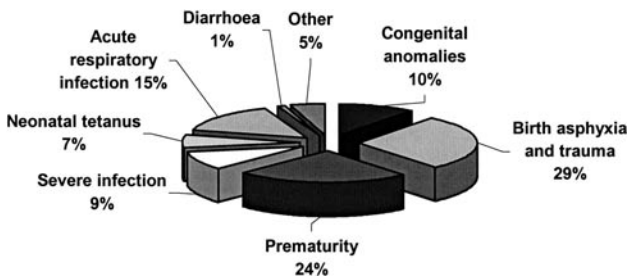

Figure 1. Causes of neonatal mortality.

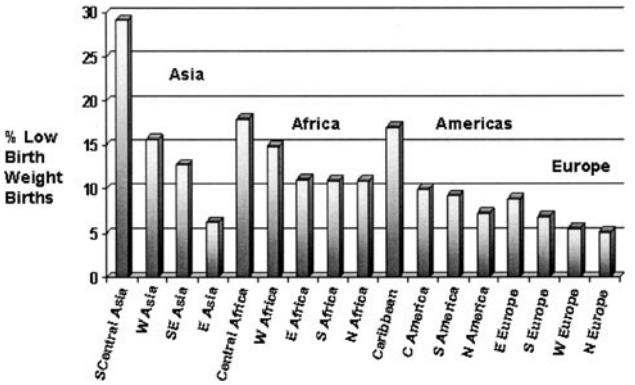

Figure 2. Subregional estimates of low birth weight.

Maternal infections with syphilis, HIV, and malaria also add to the fetal and newborn deaths and morbidity. Data from Matlab, Bangladesh (with demographic surveillance ongoing since the 1960s) also show that a large proportion of perinatal mortality is due to complications in childbirth (Table 2).[16]

Programs such as the tetanus immunization and Baby Friendly Hospital Initiative have successfully reduced some of the mortality burden — but integrated essential service delivery before and during pregnancy, childbirth, and after delivery is urgently needed. Although preventive care should begin before pregnancy, with access to family planning to delay childbearing until social and biological maturity, care in pregnancy, during childbirth, and in the first days after delivery are critical for the care of the baby and the mother. In most of the world, women do not have access to antenatal and postpartum care, even less to skilled care for childbirth. The cost of investment in maternity services is moderate but it pays off in big returns as reduced maternal and perinatal mortality.

Action is urgently needed to expand these services to ensure safer pregnancies and births and to reduce deaths in mothers and their children. Ensuring skilled health care at birth is a crucially important measure. In order to have one day an attendant with

Table 2 Causes of Perinatal Mortality Matlab, Bangladesh (1987–1993)

	Antenatal markers*	Preterm birth (<37 weeks)	Labor complications†
Prevalence	42	20	12
Perinatal mortality	100	148	220
Odds ratio	2 (1.5–2.6)	3.4 (2.6–4.4)	5.4 (4.1–7.1)
Population attributable risk (%)	26	27	30

Modified from Ref. 16.

*Antenatal markers include: maternal age ≤18 years, bad obstetric history, maternal upper arm circumference ≥250 mm, maternal weight = 10th percentile for gestational age, preeclampsia, jaundice.

†Labor complications include: breech or other malpresentation, prolonged or obstructed labor, eclampsia.

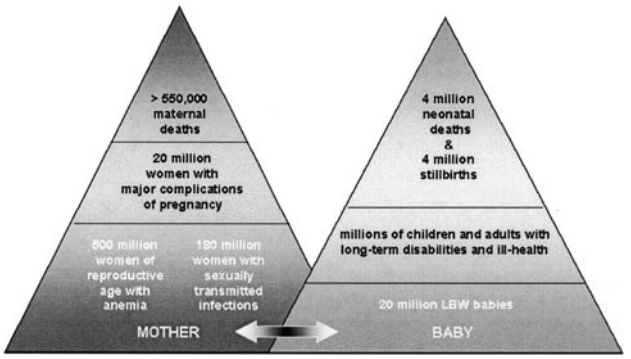

Figure 3. Related outcomes for the mother and baby.

midwifery skills for every birth, countries must start working toward this goal today. In the interim, they may look into alternatives. When the resources are most limited, focusing on maternal tetanus immunization, promoting, protecting, and supporting early and exclusive breast-feeding and ensuring clean practices around birth can already make a difference.

LINKS WITH SAFE MOTHERHOOD

Anne Tinker, Joy Lawn

The health of mothers and that of their infants and children are intimately related (Figure 3). Half a million women die each year of pregnancy-related causes,[17] but 20 million more suffer long-term complications resulting from childbearing.[18] Still another 500 million suffer from pregnancy-induced anemia,[19] and 180 million live with the spectra of sexually transmitted diseases.[18] This level of morbidity leaves women less able to care for themselves and their families and less able to bear the stress of further pregnancies. When women get sick or die, their children — especially their daughters — often suffer and also die.[20]

Keys to ensuring women's health are family planning and nutritional support, quality antenatal and postpartum care, and skilled health care at birth including management of complications. These interventions also directly benefit newborn health and survival. The USAID-funded Demographic Health Surveys estimate that improving birth spacing in India to greater than 2 years would reduce infant mortality by over 25%.[1] This translates into a reduction of half a million deaths per year in India alone.[21] Improving the health of newborns is an important step in advancing societal transition from high infant mortality and high fertility to low mortality and low fertility.

Importantly, recent studies have shown that a reduced number of antenatal visits can produce similar birth outcomes compared with a multiple-visit model, while often reducing cost for implementing organizations.[21] Central to the success of this new model of prenatal care is careful control of the content of care and the duration of consultation. Both women and newborns benefit directly from presumptive antenatal treatment of malaria and identification and treatment of sexually transmitted infections. For example, it has been estimated that for a population of 40,000 pregnant women with a syphilis seroprevalence of over 5%, treatment would reduce maternal morbidity and mortality from syphilis, but would also prevent 400 spontaneous abortions, 600 late fetal deaths, 250 preterm births, and 500 cases of congenital syphilis.[22]

Women's socioeconomic status is also an important predictor of her fertility, access to prenatal care, and skilled health care at delivery. World Bank estimates from seven countries show that the poorest women have the most children, but the least access to care.[23] Women's low status within the community and family is also an important factor to consider when designing interventions to improve maternal and neonatal health. Often women are not the primary decision makers regarding their own health care or the care of their children; programs attempting to change care-seeking behaviors must therefore target mothers-in-law and husbands as well as women of childbearing age.

As essential service packages are designed and tested, it is important to examine cost-effectiveness and feasibility, as well as intervention efficacy. Packages should also be responsive to local needs and be adaptable enough to be fine-tuned to local conditions as implementation proceeds. Strategies should emphasize recognition of the danger signs of serious illness, and discourage the use of harmful traditional practices, such as ''eating down'' in the last trimester, which contributes to the problem of LBW. Programs must also address referral of complicated illness as well as removal of the barriers to referral (e.g., transportation, money, child care, lack of decision-making power). Some successful programs have been launched by collaborations of many partners, and bridge the gaps from the family and community levels to the national and international levels. Only when the community is vested in the health of women and children will we be able to sustain a reduction in their burden of preventable deaths.